

10527127.trn

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PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America  
NEWS 2 JAN 08 CHEMLIST enhanced with New Zealand Inventory of Chemicals  
NEWS 3 JAN 16 CA/CAPLUS Company Name Thesaurus enhanced and reloaded  
NEWS 4 JAN 16 IPC version 2007.01 thesaurus available on STN  
NEWS 5 JAN 16 WPIDS/WPINDEX/WPIX enhanced with IPC 8 reclassification data  
NEWS 6 JAN 22 CA/CAPLUS updated with revised CAS roles  
NEWS 7 JAN 22 CA/CAPLUS enhanced with patent applications from India  
NEWS 8 JAN 29 PHAR reloaded with new search and display fields  
NEWS 9 JAN 29 CAS Registry Number crossover limit increased to 300,000 in  
multiple databases  
NEWS 10 FEB 15 PATDPASPC enhanced with Drug Approval numbers  
NEWS 11 FEB 15 RUSSIAPAT enhanced with pre-1994 records  
NEWS 12 FEB 23 KOREAPAT enhanced with IPC 8 features and functionality  
NEWS 13 FEB 26 MEDLINE reloaded with enhancements  
NEWS 14 FEB 26 EMBASE enhanced with Clinical Trial Number field  
NEWS 15 FEB 26 TOXCENTER enhanced with reloaded MEDLINE  
NEWS 16 FEB 26 IFICDB/IFIPAT/IFIUDB reloaded with enhancements  
NEWS 17 FEB 26 CAS Registry Number crossover limit increased from 10,000  
to 300,000 in multiple databases  
NEWS 18 MAR 15 WPIDS/WPIX enhanced with new FRAGHITSTR display format  
NEWS 19 MAR 16 CASREACT coverage extended  
NEWS 20 MAR 20 MARPAT now updated daily  
NEWS 21 MAR 22 LWPI reloaded  
NEWS 22 MAR 30 RDISCLOSURE reloaded with enhancements  
NEWS 23 MAR 30 INPADOCDB will replace INPADOC on STN  
NEWS 24 APR 02 JICST-EPLUS removed from database clusters and STN  
  
NEWS EXPRESS NOVEMBER 10 CURRENT WINDOWS VERSION IS V8.01c, CURRENT  
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
AND CURRENT DISCOVER FILE IS DATED 25 SEPTEMBER 2006.  
  
NEWS HOURS STN Operating Hours Plus Help Desk Availability  
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NEWS IPC8 For general information regarding STN implementation of IPC 8

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FILE 'HOME' ENTERED AT 11:52:35 ON 27 APR 2007

=>

Uploading

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE

Do you want to switch to the Registry File?

Choice (Y/n):

Switching to the Registry File...

Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

=> FILE REGISTRY

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 11:52:48 ON 27 APR 2007

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STRUCTURE FILE UPDATES: 26 APR 2007 HIGHEST RN 933069-51-3

DICTIONARY FILE UPDATES: 26 APR 2007 HIGHEST RN 933069-51-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

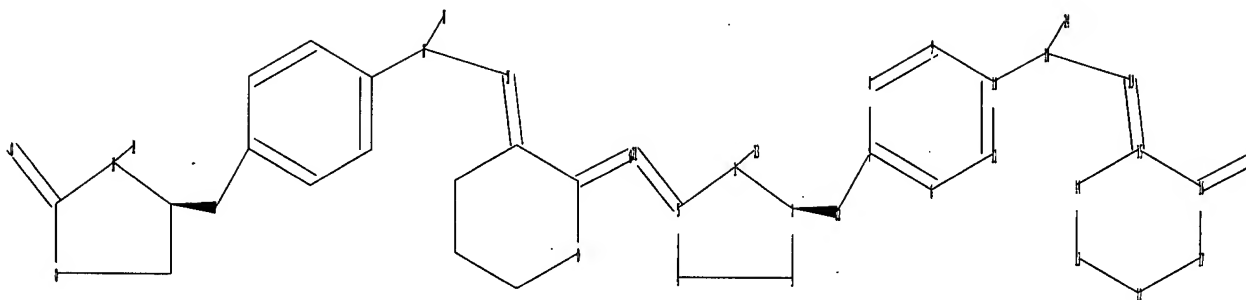
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REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>

Uploading C:\Program Files\Stnexp\Queries\10527127.str



chain nodes :

18 19 20 21 22 23 24

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17

chain bonds :

1-23 2-22 5-21 7-22 10-18 15-19 16-20 18-19 18-24

ring bonds :

1-2 1-5 2-3 3-4 4-5 6-7 6-11 7-8 8-9 9-10 10-11 12-13 12-17 13-14  
14-15 15-16 16-17

exact/norm bonds :

1-2 1-5 5-21 10-18 15-19 16-20 18-19

exact bonds :

1-23 2-3 2-22 3-4 4-5 7-22 12-13 12-17 13-14 14-15 15-16 16-17 18-24

normalized bonds :

6-7 6-11 7-8 8-9 9-10 10-11

isolated ring systems :

containing 1 : 6 : 12 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS  
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS

Stereo Bonds:

22-2 (Single Wedge).

Stereo Chiral Centers:

2 (Parity=Don't Care)

Stereo RSS Sets:

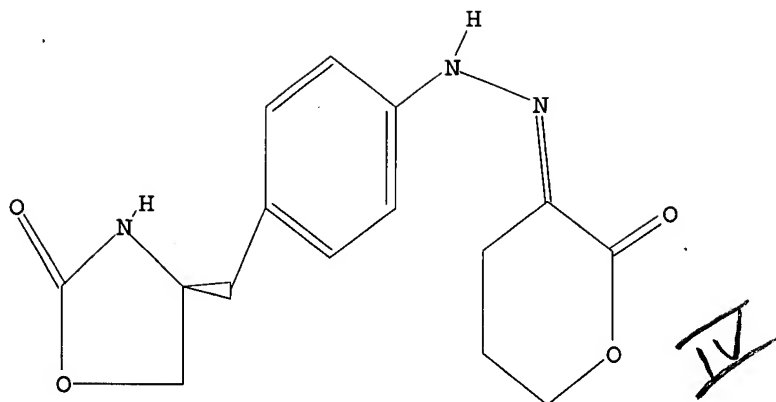
Type=Relative (Default). 1 Nodes= 2

L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1

SAMPLE SEARCH INITIATED 11:53:06 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 0 TO 0

PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 11:53:12 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS

SEARCH TIME: 00.00.01

1 ANSWERS

L3 1 SEA SSS FUL L1

=> FIL HCAPLUS

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

172.10

172.31

FILE 'HCAPLUS' ENTERED AT 11:53:21 ON 27 APR 2007

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FILE COVERS 1907 - 27 Apr 2007 VOL 146 ISS 19  
FILE LAST UPDATED: 26 Apr 2007 (20070426/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

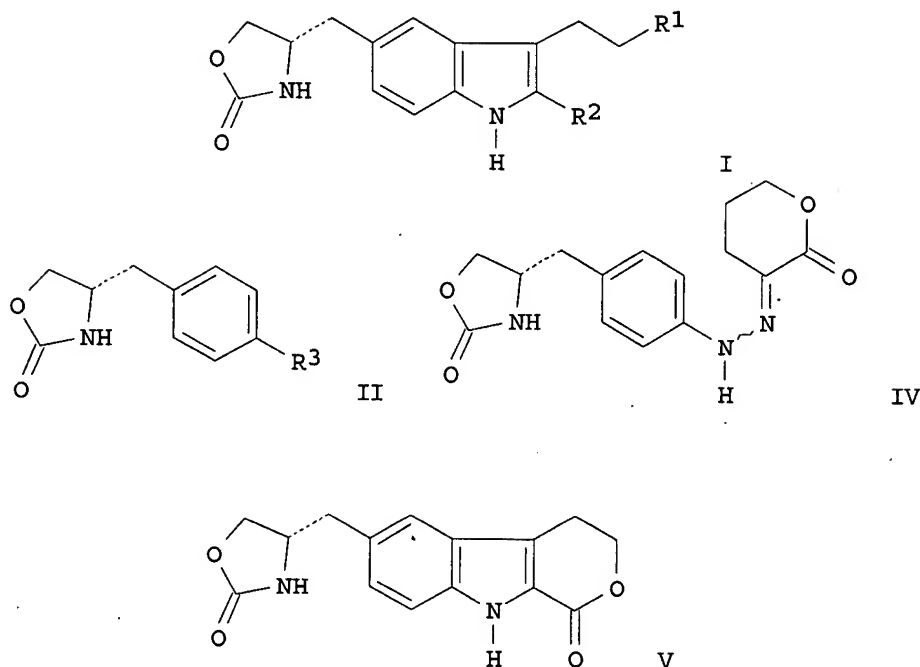
=> s l3

L4 1 L3

=> d l4 ibib abs hitstr tot

L4 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN  
ACCESSION NUMBER: 2004:143143 HCAPLUS  
DOCUMENT NUMBER: 140:181327  
TITLE: Process for the preparation of zolmitriptan compounds  
via ~~Elscher~~ indole synthesis  
INVENTOR(S): Dalmases Barjoan, Pere; Armengol Asparo, Montserrat  
PATENT ASSIGNEE(S): Laboratorios Vita, S. A., Spain  
SOURCE: PCT Int. Appl., 29 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014901	A1	20040219	WO 2003-IB3536	20030805
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
ES 2204302	A1	20040416	ES 2002-1873	20020807
ES 2204302	B2	20050301		
AU 2003250476	A1	20040225	AU 2003-250476	20030805
EP 1534705	A1	20050601	EP 2003-784403	20030805
EP 1534705	B1	20060726		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
AT 334126	T	20060815	AT 2003-784403	20030805
NO 2005001178	A	20050304	NO 2005-1178	20050304
US 2006025600	A1	20060202	US 2005-527127	20050308
PRIORITY APPLN. INFO.:			ES 2002-1873	A 20020807
			WO 2003-IB3536	W 20030805
OTHER SOURCE(S):	CASREACT 140:181327; MARPAT 140:181327			
GI				



AB The invention relates to zolmitriptan I ( $R_1 = \text{NMe}_2$ ,  $R_2 = \text{H}$ ) and a pharmaceutically acceptable salt thereof prepared from (aminobenzyl)oxazolidinone II•HCl ( $R_3 = \text{NH}_2$ ) via (a) preparation of hydrazine III (II,  $R_3 = \text{NHNH}_2$ ) and subsequent in situ reaction of the hydrazine III with  $\alpha$ -keto- $\delta$ -valerolactone, to give the hydrazone IV; (b) submission of the hydrazone IV to the Fischer indole synthesis to give the pyranoindolone of formula V; (c) transesterification of the pyranoindolone V to provide indole VI (I,  $R_1 = \text{OH}$ ,  $R_2 = -\text{CO}_2\text{-alkyl}$ , alkyl = C1-C4); (d) conversion of the hydroxyl group of the compound VI into dimethylamino to give the indolecarboxylate VII (I,  $R_1 = \text{NMe}_2$ ,  $R_2 = -\text{CO}_2\text{-alkyl}$ , alkyl = C1-C4); (e) saponification of the VII to provide indolecarboxylic acid VIII (I,  $R_1 = \text{NMe}_2$ ,  $R_2 = \text{CO}_2\text{H}$ ); and (f) decarboxylation of VIII. Prior methods for the preparation of zolmitriptan compds. are either not applicable at industrial scale or require a stage of column purification of the end product, and may also use toxic reagents such as tin chloride for preparing the hydrazine, while having an overall yield of only 18%. For instance, zolmitriptan I ( $R_1 = \text{NMe}_2$ ,  $R_2 = \text{H}$ ) was prepared via 6 steps with 87-95% yield for each step (alkyl is ethyl).

IT 659738-63-3P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (process intermediate; preparation of zolmitriptan from [(pyranilidenhydrazino)benzyl]oxazolidinone via Fischer indole synthesis, transesterification, amination of hydroxy, saponification, and decarboxylation)

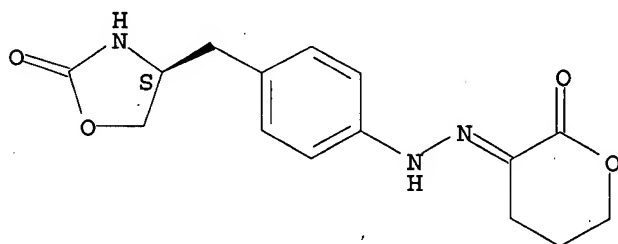
RN 659738-63-3 HCAPLUS

CN 2H-Pyran-2,3(4H)-dione, dihydro-, 3-[[4-[[[(4S)-2-oxo-4-oxazolidinyl]methyl]phenyl]hydrazone] (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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Double bond geometry unknown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> FIL REGISTRY  
COST IN U.S. DOLLARS

SINCE FILE	TOTAL
ENTRY	SESSION
18.27	190.58

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
-0.78	-0.78

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STRUCTURE FILE UPDATES: 26 APR 2007 HIGHEST RN 933069-51-3  
DICTIONARY FILE UPDATES: 26 APR 2007 HIGHEST RN 933069-51-3

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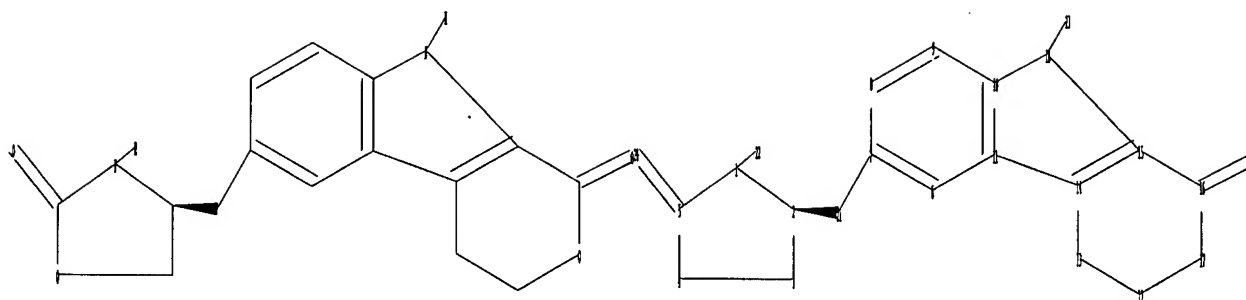
TSCA INFORMATION NOW CURRENT THROUGH December 2, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

=>  
Uploading C:\Program Files\Stnexp\Queries\10527127a.str



chain nodes :

19 20 21 22 23

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18

chain bonds :

1-22 2-21 5-20 7-21 16-19 18-23

ring bonds :

1-2 1-5 2-3 3-4 4-5 6-7 6-11 7-8 8-9 9-10 10-11 10-18 11-14 12-13  
12-17 13-14 14-15 15-16 15-18 16-17

exact/norm bonds :

1-2 1-5 5-20 10-18 15-18 16-19

exact bonds :

1-22 2-3 2-21 3-4 4-5 7-21 11-14 12-13 12-17 13-14 14-15 15-16 16-17  
18-23

normalized bonds :

6-7 6-11 7-8 8-9 9-10 10-11

isolated ring systems :

containing 1 : 6 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:CLASS 19:CLASS  
20:CLASS 21:CLASS 22:CLASS 23:CLASS

Stereo Bonds:

21-2 (Single Wedge).

Stereo Chiral Centers:

2 (Parity=Don't Care)

Stereo RSS Sets:

Type=Relative (Default). 1 Nodes= 2

L5 STRUCTURE UPLOADED

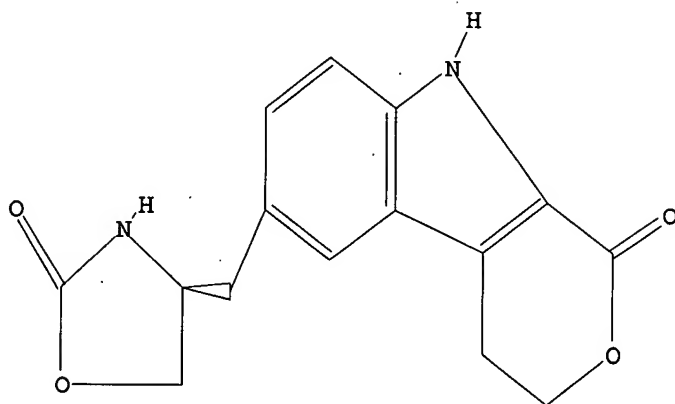
=> d 15

L5 HAS NO ANSWERS

L5 STR



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*Formula*  
*(✓)*

Structure attributes must be viewed using STN Express query preparation.

=> s 15

SAMPLE SEARCH INITIATED 11:56:29 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 2 TO ITERATE

100.0% PROCESSED 2 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.02

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 2 TO 124

PROJECTED ANSWERS: 0 TO 0

L6 0 SEA SSS SAM L5

=> s 15 sss full

FULL SEARCH INITIATED 11:56:36 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 102 TO ITERATE

100.0% PROCESSED 102 ITERATIONS

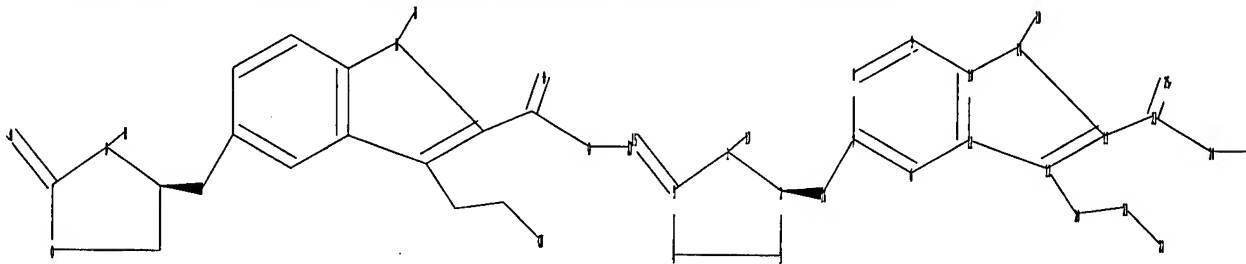
1 ANSWERS

SEARCH TIME: 00.00.01

L7 1 SEA SSS FUL L5

=>

Uploading C:\Program Files\Stnexp\Queries\10527127b.str



chain nodes :

10527127.trn

15 16 17 18 20 21 22 23 24 25 26  
ring nodes :  
1 2 3 4 5 6 7 8 9 10 11 12 13 14  
chain bonds :  
1-17 2-16 5-15 7-16 12-20 13-23 14-18 20-21 21-22 23-24 23-25 24-26  
ring bonds :  
1-2 1-5 2-3 3-4 4-5 6-7 6-11 7-8 8-9 9-10 10-11 10-14 11-12 12-13  
13-14  
exact/norm bonds :  
1-2 1-5 5-15 10-14 13-14 21-22 23-24 23-25 24-26  
exact bonds :  
1-17 2-3 2-16 3-4 4-5 7-16 11-12 12-13 12-20 13-23 14-18 20-21  
normalized bonds :  
6-7 6-11 7-8 8-9 9-10 10-11  
isolated ring systems :  
containing 1 : 6 :

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
11:Atom 12:Atom 13:Atom 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS  
20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS

Stereo Bonds:

16-2 (Single Wedge).

Stereo Chiral Centers:

2 (Parity=Don't Care)

Stereo RSS Sets:

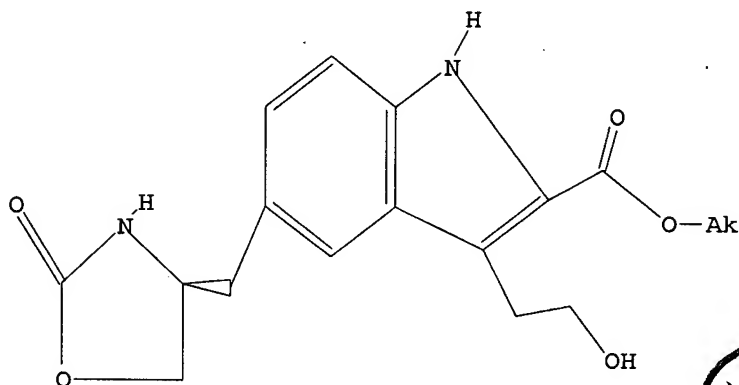
Type=Relative (Default). 1 Nodes= 2

L8 STRUCTURE UPLOADED

=> d 18

L8 HAS NO ANSWERS

L8 STR



Structure attributes must be viewed using STN Express query preparation.

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=> s l8

SAMPLE SEARCH INITIATED 11:59:31 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED 1 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 1 TO 80

PROJECTED ANSWERS: 0 TO 0

L9 0 SEA SSS SAM L8

=> s l8 sss full

FULL SEARCH INITIATED 11:59:37 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 9 TO ITERATE

100.0% PROCESSED 9 ITERATIONS

2 ANSWERS

SEARCH TIME: 00.00.01

L10 2 SEA SSS FUL L8

=> FIL HCAPLUS

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

346.00

536.58

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

0.00

-0.78

FILE 'HCAPLUS' ENTERED AT 11:59:42 ON 27 APR 2007

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FILE COVERS 1907 - 27 Apr 2007 VOL 146 ISS 19

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=> d his

(FILE 'HOME' ENTERED AT 11:52:35 ON 27 APR 2007)

FILE 'REGISTRY' ENTERED AT 11:52:48 ON 27 APR 2007

L1 STRUCTURE UPLOADED  
L2 0 S L1  
L3 1 S L1 SSS FULL

FILE 'HCAPLUS' ENTERED AT 11:53:21 ON 27 APR 2007

L4 1 S L3

FILE 'REGISTRY' ENTERED AT 11:56:10 ON 27 APR 2007

L5 STRUCTURE UPLOADED  
L6 0 S L5  
L7 1 S L5 SSS FULL  
L8 STRUCTURE UPLOADED  
L9 0 S L8  
L10 2 S L8 SSS FULL

FILE 'HCAPLUS' ENTERED AT 11:59:42 ON 27 APR 2007

=&gt; s 17

L11 1 L7

=&gt; s 110

L12 1 L10

=&gt; d l11 ibib abs hitstr tot

L11 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2004:143143 HCAPLUS

DOCUMENT NUMBER: 140:181327

TITLE: Process for the preparation of zolmitriptan compounds  
via Fischer indole synthesis

INVENTOR(S): Dalmases Barjoan, Pere; Armengol Asparó, Montserrat

PATENT ASSIGNEE(S): Laboratorios Vita, S. A., Spain

SOURCE: PCT Int. Appl., 29 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014901	A1	20040219	WO 2003-IB3536	20030805
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
ES 2204302	A1	20040416	ES 2002-1873	20020807
ES 2204302	B2	20050301		
AU 2003250476	A1	20040225	AU 2003-250476	20030805
EP 1534705	A1	20050601	EP 2003-784403	20030805
EP 1534705	B1	20060726		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

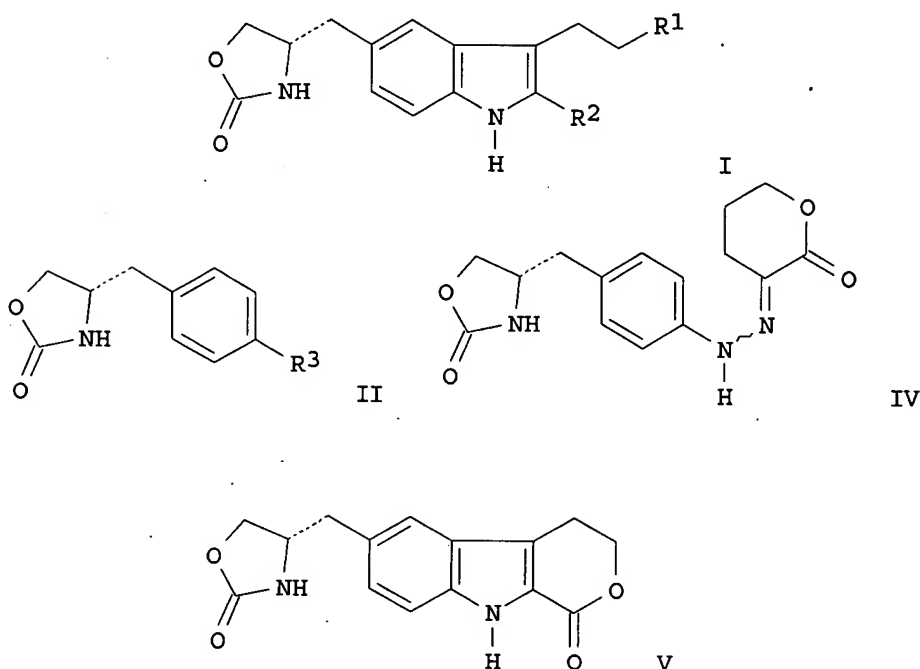
AT 334126	T	20060815	AT 2003-784403	20030805
NO 2005001178	A	20050304	NO 2005-1178	20050304
US 2006025600	A1	20060202	US 2005-527127	20050308

PRIORITY APPLN. INFO.:

ES 2002-1873	A	20020807
WO 2003-IB3536	W	20030805

OTHER SOURCE(S):  
GI

CASREACT 140:181327; MARPAT 140:181327



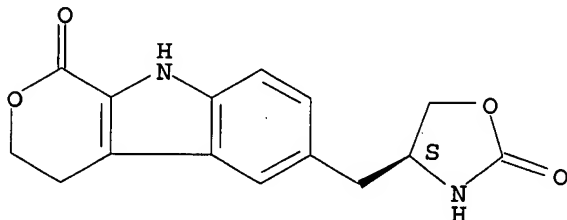
- AB The invention relates to zolmitriptan I (R1 = NMe2, R2 = H) and a pharmaceutically acceptable salt thereof prepared from (aminobenzyl)oxazolidinone II•HCl (R3 = NH2) via (a) preparation of hydrazine III (II, R3 = NHNH2) and subsequent in situ reaction of the hydrazine III with  $\alpha$ -keto- $\delta$ -valerolactone, to give the hydrazone IV; (b) submission of the hydrazone IV to the Fischer indole synthesis to give the pyranoindolone of formula V; (c) transesterification of the pyranoindolone V to provide indole VI (I, R1 = OH, R2 = -CO2-alkyl, alkyl = C1-C4); (d) conversion of the hydroxyl group of the compound VI into dimethylamino to give the indolecarboxylate VII (I, R1 = NMe2, R2 = -CO2-alkyl, alkyl = C1-C4); (e) saponification of the VII to provide indolecarboxylic acid VIII (I, R1 = NMe2, R2 = CO2H); and (f) decarboxylation of VIII. Prior methods for the preparation of zolmitriptan compds. are either not applicable at industrial scale or require a stage of column purification of the end product, and may also use toxic reagents such as tin chloride for preparing the hydrazine, while having an overall yield of only 18%. For instance, zolmitriptan I (R1 = NMe2, R2 = H) was prepared via 6 steps with 87-95% yield for each step (alkyl is ethyl).
- IT 659738-65-5P, (S)-6-(2-Oxo-1,3-oxazolidin-4-ylmethyl)-4,9-dihydro-3H-pyrano-[3,4-b]indol-1-one

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (process intermediate; preparation of zolmitriptan from [(pyranilidenhydrazino)benzyl]oxazolidinone via Fischer indole synthesis, transesterification, amination of hydroxy, saponification, and decarboxylation)

RN 659738-65-5 HCAPLUS

CN Pyrano[3,4-b]indol-1(3H)-one, 4,9-dihydro-6-[[[(4S)-2-oxo-4-oxazolidinyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L12 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2007 ACS on SPN

ACCESSION NUMBER: 2004:143143 HCAPLUS

DOCUMENT NUMBER: 140:181327

TITLE: Process for the preparation of zolmitriptan compounds via Fischer indole synthesis

INVENTOR(S): Dalmases Barjoan, Pere; Armengol Asparo, Montserrat

PATENT ASSIGNEE(S): Laboratorios Vita, S. A., Spain

SOURCE: PCI Int. Appl., 29 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

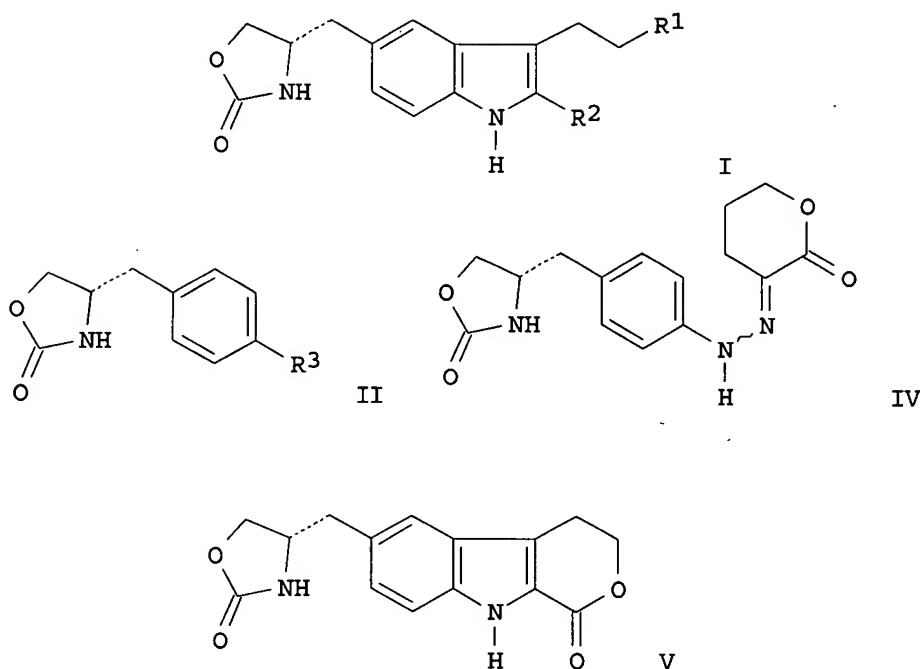
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014901	A1	20040219	WO 2003-IB3536	20030805
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
ES 2204302	A1	20040416	ES 2002-1873	20020807
ES 2204302	B2	20050301		
AU 2003250476	A1	20040225	AU 2003-250476	20030805
EP 1534705	A1	20050601	EP 2003-784403	20030805
EP 1534705	B1	20060726		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK  
 AT 334126 T 20060815 AT 2003-784403 20030805  
 NO 2005001178 A 20050304 NO 2005-1178 20050304  
 US 2006025600 A1 20060202 US 2005-527127 20050308  
 PRIORITY APPLN. INFO.: ES 2002-1873 A 20020807  
 WO 2003-IB3536 W 20030805  
 OTHER SOURCE(S): CASREACT 140:181327; MARPAT 140:181327  
 GI



- AB The invention relates to zolmitriptan I (R<sup>1</sup> = NMe<sub>2</sub>, R<sup>2</sup> = H) and a pharmaceutically acceptable salt thereof prepared from (aminobenzyl)oxazolidinone II•HCl (R<sup>3</sup> = NH<sub>2</sub>) via (a) preparation of hydrazine III (II, R<sup>3</sup> = NHNH<sub>2</sub>) and subsequent in situ reaction of the hydrazine III with α-keto-δ-valerolactone, to give the hydrazone IV; (b) submission of the hydrazone IV to the Fischer indole synthesis to give the pyranoindolone of formula V; (c) transesterification of the pyranoindolone V to provide indole VI (I, R<sup>1</sup> = OH, R<sup>2</sup> = -CO<sub>2</sub>-alkyl, alkyl = C<sub>1</sub>-C<sub>4</sub>); (d) conversion of the hydroxyl group of the compound VI into dimethylamino to give the indolecarboxylate VII (I, R<sup>1</sup> = NMe<sub>2</sub>, R<sup>2</sup> = -CO<sub>2</sub>-alkyl, alkyl = C<sub>1</sub>-C<sub>4</sub>); (e) saponification of the VII to provide indolecarboxylic acid VIII (I, R<sup>1</sup> = NMe<sub>2</sub>, R<sup>2</sup> = CO<sub>2</sub>H); and (f) decarboxylation of VIII. Prior methods for the preparation of zolmitriptan compds. are either not applicable at industrial scale or require a stage of column purification of the end product, and may also use toxic reagents such as tin chloride for preparing the hydrazine, while having an overall yield of only 18%. For instance, zolmitriptan I (R<sup>1</sup> = NMe<sub>2</sub>, R<sup>2</sup> = H) was prepared via 6 steps with 87-95% yield for each step (alkyl is ethyl).
- IT 659738-67-7P, (S)-3-(2-Hydroxyethyl)-5-(2-oxo-1,3-oxazolidin-4-ylmethyl)-1H-indol-2-carboxylic acid ethyl ester

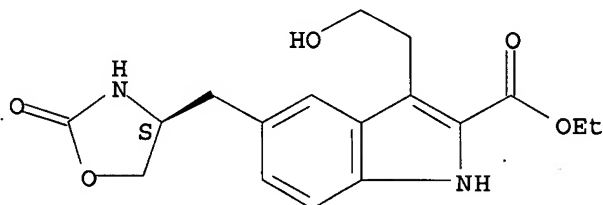
10527127.trn

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (process intermediate; preparation of zolmitriptan from [(pyranilidenhydrazino)benzyl]oxazolidinone via Fischer indole synthesis, transesterification, amination of hydroxy, saponification, and decarboxylation)

RN 659738-67-7 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 3-(2-hydroxyethyl)-5-[[[(4S)-2-oxo-4-oxazolidinyl]methyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



IT 659738-66-6P, (S)-3-(2-Hydroxyethyl)-5-(2-oxo-1,3-oxazolidin-4-ylmethyl)-1H-indol-2-carboxylic acid methyl ester

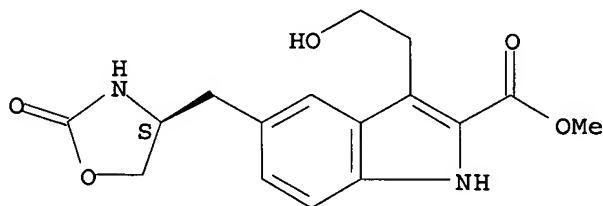
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)

(process intermediate; preparation of zolmitriptan from [(pyranilidenhydrazino)benzyl]oxazolidinone via Fischer indole synthesis, transesterification, amination of hydroxy, saponification, and decarboxylation)

RN 659738-66-6 HCAPLUS

CN 1H-Indole-2-carboxylic acid, 3-(2-hydroxyethyl)-5-[[[(4S)-2-oxo-4-oxazolidinyl]methyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

15.74

552.32

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-1.56

-2.34

STN INTERNATIONAL LOGOFF AT 12:00:37 ON 27 APR 2007